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910000-2020**REMARKS**

Examiner Yu is thanked for courtesies extended during the telephonic interview of July 9, 2003. Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the amendments and remarks herewith, which place the application into condition for allowance.

**I. Status of the Claims and Formal Matters**

Claims 1-7, and 16-29 are under examination in this application. Claims 1, 2, 6, 16, and 17 have been amended. Applicants acknowledge the final restriction requirement in the Office Action of March 26, 2003, and Claims 8-15 are canceled, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents. Applicants reserve the right to file divisional applications to pursue the full scope of the claims.

No new matter has been added by these amendments. Support is found throughout the specification and from the pending claims. Specifically, support for the recitation of Claims 1 and 16 can be found on page 3, lines 18-25 of the instant application.

Applicants acknowledge withdrawal of previous rejections under 35 U.S.C. § 112, first paragraph and withdrawal of the previous rejection in view of the oath and declaration submitted in the amendment and response filed on November 25, 2002 and November 27, 2002. The Examiner is thanked for consideration of arguments and actions taken accordingly.

It is submitted that the claims, herewith and as originally presented, are in full compliance with the requirements of 35 U.S.C. §§ 112 and 119(e). The amendments to the claims herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 112 or 119(e); but rather the addition and amendments to the claims are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

**Priority Claim**

The objection to the domestic priority claim under 35 U.S.C. § 119(e) based on provisional application No. 60/127,221 ("the '221 application") is respectfully traversed. The '221 application discloses a method of treating a subject with a disorder characterized by unwanted cell proliferation by increasing expression of TSP-2. As disclosed on pages 5 and 18

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of the '221 application, this can be accomplished by introducing into the subject a genetically modified cell that expresses the molecule. The '221 application states on page 39 that the gene therapy construct "can comprise a slow release matrix in which the gene delivery vehicle is imbedded." Such a matrix is encompassed by that of the instant application, which states on page 11 "[b]ioactive materials may also be incorporated into the device or a sustained release matrix within the device to promote cell viability or proliferation."

The Examiner indicated, during the telephonic interview of July 9, 2003, that the rejection under 35 U.S.C. §119(e), regarding the terms "slow release matrix" in the '221 application and "sustained release matrix" in the instant application, was overcome. Therefore, Applicants respectfully request that the objection to the claim of domestic priority under 35 U.S.C. § 119(e) be formally withdrawn.

**II. The Enablement Rejection Under 35 U.S.C. §112, 1<sup>st</sup> Paragraph, Is Overcome**

Claims 1-7 and 16-29 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. The rejection is respectfully traversed.

The Office Action contends that the instant application does not reasonably provide enablement for anti-angiogenic molecules other than TSP-2. However, the Applicants counter that it is well within the purview of the skilled artisan, in an area in which the skill of one in the art is quite high, to identify diseases that are treatable with anti-angiogenic molecules and to treat such diseases using the cell-matrix structure of the invention. This is especially true in view of the amendments presented herewith, which have directed the scope of the claims to diseases that are treatable by anti-angiogenic molecules. Thus, any person of ordinary skill in the art would have a reasonable expectation of success, and as such, it would not require undue experimentation to practice the full scope of the instant invention as claimed.

The Office Action further asserts that the specification does not teach that any anti-angiogenic molecule other than thrombospondin-2 (TSP-2) may be used in the methods of the invention. The use of TSP-2 is exemplified, however, it is explicitly stated that other anti-angiogenic molecules, such as those described in the claimed subject matter, can be used at several places in the application. For example, on page 7, line 15, the application reads, "Any biologically active anti-angiogenic molecule which has been cloned or for which a cellular source is available can be used." Additionally, TSP-1, endostatin, and angiostatin are supported

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in the specification on page 7, lines 29-31. The arguments offered in the Amendment filed on November 22, 2002 are restated here.

It would appear that the Examiner's rejection is based on the fact that the Examples exemplify data obtained using TSP-2 and not other anti-angiogenic molecules described in the specification, such as TSP-1, thrombomodulin, angiostatin and endostatin.<sup>1</sup> As stated in MPEP 2164.02, "[t]he presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure... To make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims." MPEP 2164.02 continues to say, "[p]roof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation." Such evidence has not been provided here.

During the interview of July 9, 2003, it was expressed that the Applicants are understood to be the first to express anti-angiogenic molecules in an implantable cell-matrix structure to treat diseases, which are treatable by the anti-angiogenic molecules and characterized by excessive proliferation of tissue as claimed in the instant application.

Therefore, reconsideration and withdrawal of the enablement rejections under 35 U.S.C. §112, 1<sup>st</sup> Paragraph, are respectfully requested.

### **III. The Double Patenting Rejection is Overcome**

Claim 26 was objected to under 37 C.F.R. 1.75 as being a substantial duplicate of claim 6. Claim 6 has been amended, such that it is now directed to TSP-2; Claim 26 is directed to thrombomodulin. Therefore, the claims encompass distinct subject matter, rendering this rejection moot. Reconsideration and withdrawal of the double patenting rejection is therefore respectfully requested.

<sup>1</sup> On page 4, the Office Action alleges that "[t]he specification discloses a method of treatment comprising implanting a cell-matrix structure with attached cells, which express a gene encoding TSP-2, but not thrombomodulin or any other molecule. There is no teaching or exemplification in the specification indicating that thrombomodulin or any molecule other than TSP-2 may be used in the method as claimed."

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910000-2020**IV. The Written Description Rejection Under 35 U.S.C. §112, 1<sup>st</sup> Paragraph, Is****Overcome**

Claims 27-29 were rejected under 35 U.S.C. §112, 1<sup>st</sup> Paragraph, as allegedly lacking adequate written description. The rejection is respectfully traversed.

The Office Action states that support for the anti-angiogenic molecules recited in claims 27-29 cannot be found in the application. The Examiner's attention is respectfully directed to page 7, lines 28-31 of the specification, wherein TSP-1, angiostatin, and endostatin are disclosed as anti-angiogenic molecules. The Examiner acknowledged as much in the telephonic interview of July 9, 2003, and indicated that she would broaden the scope of her search to encompass endostatin and angiostatin, under the genus of anti-angiogenic molecules encompassed by claim 1.

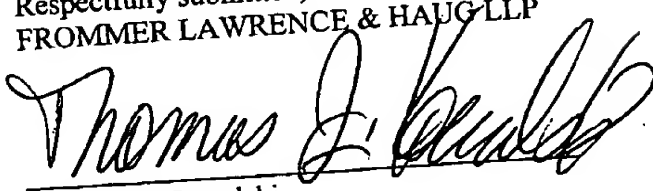
Accordingly, reconsideration and withdrawal of the written description rejection under 35 U.S.C. § 112, 1<sup>st</sup> paragraph, is respectfully requested.

**CONCLUSION**

In view of the remarks and amendments herewith, the application is believed to be in condition for allowance, or at least in better condition for appeal. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date.

Respectfully submitted,  
FROMMER LAWRENCE & HAUG LLP

By:



Thomas J. Kowalski  
Reg. No. 32,147

Anne-Marie C. Yvon, Ph.D.  
Reg. No. 52,390  
(212) 588-0800

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